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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,664	02/18/2004	Felix A. Montero-Julian	BECK1130-2(2052-183)	5199

47975 7590 01/24/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,664	MONTERO-JULIAN ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11,13-17,20-34,36,38-42 and 45-78* is/are pending in the application.

4a) Of the above claim(s) *7,8,15,16,23,24,32,33,39-41,48,49,51-72 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,11,13,14,17,20-22,25-31,34,36,38,42,45-47,50 and 73-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/12/07 & 10/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 10/17/07 is acknowledged and has been entered.

2. Applicant's election of Group I , and species of HLA-A2/β2m/MART-1 as the MHC/template peptide complex in Applicant's responses filed 3/27/07 and 11/13/06 is acknowledged. In addition, Applicant's election of the species 100X molar excess of competitor peptide, incubating the sample for about 2-20 hours at about 21 degrees C, HBc 18-27 tagged with FITC as the tracer peptide, only one competitor peptide is used and soluble HLA molecule in Applicant's response filed 3/27/07 is acknowledged.

Claims 1-6, 9, 11, 13, 14, 17, 20-22, 25-31, 34, 36, 38, 42, 45-47, 50 and 73-77 read on the elected species.

Accordingly, claims 7, 8, 15, 16, 23, 24, 32, 33, 39, 40, 41, 48, 49, 78 (non-elected species of Group I) and claims 51-72 (non-elected Group II) remain withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-6, 9, 11, 13, 14, 17, 20-22, 25-31, 34, 36, 38, 42, 45-47, 50 and 73-77 are currently being examined.

3. Applicant's amendment of claims 1, 26 and 73 to recite "wherein the MHC monomer is HLA-A2, further comprising beta-2 microglobulin, and wherein the modified MHC monomer maintains the ability to assemble into a ternary complex with the template MHC-binding peptide and beta-2 microglobulin" has overcome the prior written description rejection of record, the 112, second paragraph rejection of record at prior item #6b, the prior 102(b) rejection of record and the prior 103(a) rejection of record.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13, 14, 38 and 73-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The new grounds of rejection at "a" and "b" below are necessitated by Applicant's amendment canceling claims 12 and 37.

a. Claim 13 is indefinite in the recitation of "The method of claim 12" because it is not clear what is meant. Claim 12 is a canceled claim.

b. Claim 38 is indefinite in the recitation of "the method of claim 37" because it is not clear what is meant. Claim 37 is a canceled claim.

c. Claims 73-77 are indefinite in the recitation of "system" because it is not clear what is meant.

The instant specification discloses expression systems constructed from control elements operably linked to MHC sequences [0068]-[0071], prokaryotic or eukaryotic systems that are one of a variety of microorganisms or cells [0068], an ELISPOT reader system [0015]. The specification further discloses "The invention provides systems, kits and assays for evaluating putative MHC-binding peptides to determine whether such fragments can be incorporated into a ternary complex with an MHC monomer or modified MHC monomer [0079]. The specification discloses at [0104] "In still another embodiment, the invention provides systems useful for identifying an MHC-binding peptide for an MHC monomer, or modified MHC monomer. The invention systems include at least one MHC monomer or modified MHC monomer having bound thereto a template MHC-binding peptide, a tracer MHC-binding peptide tagged with a detectable label, wherein the template peptide has lower affinity than the tracer peptide for the monomer. The invention system may further include an instruction for using the system."

It is clear from the instant disclosure that a "system" is not equivalent to a "kit," such kit may also comprise the same elements as the system, including instructions. The specification does not provide disclosure of what elements comprise a "system" besides the ingredients common to both a system and a kit.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-6, 9, 11, 20-22, 25-31, 34, 36, 45-47 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/07952 A1 (IDS reference filed 7/12/07) in view of US 2003/0191286 A1.

This new ground of rejection is necessitated by Applicant's amendment of the base claims 1 and 26 to recite "wherein the MHC monomer is HLA-A2" and by Applicant's submission of the said IDS reference filed 7/12/07.

WO 92/07952 A1 teaches determining the binding affinity of a candidate peptide for a specific MHC molecule (*i.e.,* MHC heavy chain and β2m) using competition between detectable agonist peptide (a peptide known to bind to MHC that may or may not be labeled with fluorophore (claims 6 and 31) such as fluoresce in (FITC) (claims 9 and 34)) and the candidate peptide (*i.e.,* a peptide that is a competitor peptide) in up to 100-fold more from the agonist peptide. WO 92/07952 A1 teaches testing one or more concentration of candidate peptide on binding of the agonist peptide. WO 92/07952 A1 teaches an incubation time between about 12 and 48 hours at, for example, 37 degrees C (*i.e.,* "about 21 degrees C) (pages 8-9 at line 32, paragraph spanning pages 7-8). WO 92/07952 A1 teaches preloading an isolated MHC glycoprotein with a homogeneous peptide preparation, the peptide chosen to be comparatively readily released by the MHC molecule (especially page 13 at lines 19-35, page 14 at lines 1-23, page 4 at the last paragraph, and claims). WO 92/07952 A1 teaches separating the bound agonist from the unbound agonist and detecting the amount of agonist bound in the complex as a function of the concentration of test compound in the reaction mixture, including coupling the agonist peptide to biotin and separating by means of coupling the complex to a solid support via linkage with streptavidin (see entire reference, especially claims).

WO 92/07952 A1 does not teach that the MHC molecule is HLA-A2

US 2003/0191286 A1 discloses making soluble MHC class I molecules, including HLA-A2, with or without endogenous peptides loaded therein, and further discloses representative HLA-A2 binding peptides of nine or ten amino acid residues in length (see entire reference, especially [0157], [0032], [0190] and claims).

It would have been prima facie obvious to one of ordinary skill in the art to have used the soluble HLA-A2 monomers disclosed by US 2003/0191286 A1 as the MHC molecule in the method taught by WO 92/07952 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 92/07952 A1 teaches a method of determining binding affinity of a candidate peptide for a specific MHC molecule, and US 2003/0191286 A1 discloses that HLA-A2 is a specific MHC molecule and further discloses methods to make soluble MHC molecules.

Although the art reference does not explicitly teach "wherein the template peptide has lower or intermediate affinity as compared with the tracer peptide for the monomer," the art reference teaches there is peptide exchange and measurement of radioactively labeled tracer peptide and also teaches that the preloaded peptide is preferably chosen to be comparatively readily released by the MHC molecule. Therefore, the claimed method appears to be similar to the method of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for

examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the method of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

With regard to the limitation recited in instant claims 4 and 29 "wherein suitable liquid phase conditions include incubating the sample for about 2 to 20 hours," the art reference teaches incubating 2 days or 48 hours, and so meets the claim limitation.

With regard to the limitation recited in instant claims 5 and 30, "wherein the suitable liquid phase conditions further include incubating the sample at about 21 degrees C," the art reference teaches incubating at room temperature of 37 degrees C, and so meets the claim limitation.

Claims 1-6, 9, 11, 20-22 and 25 are included in this rejection because the art method of measuring affinity of a peptide of interest is also identifying said peptide for binding to MHC.

With regard to the limitation recited in instant claims 3 and 28, the said limitation is not a test step. Although the art reference does not explicitly teach "wherein the tracer peptide displaces at least 90% of the template peptide in a parallel competition assay conducted in the absence of the first competitor peptide," the art reference teaches there is peptide exchange and measurement of radioactively labeled tracer peptide and also teaches that the preloaded peptide is preferably chosen to be comparatively readily released by the MHC molecule. Therefore, the claimed method appears to be similar to the method of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the method of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

8. Claims 17 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/07952 A1 (IDS reference filed 7/12/07) in view of US 2003/0191286 A1 as applied to claims 1-9, 11, 20-22, 25-34, 36, 45-47 and 50 above, and further in view of US 20040253632 A1.

The combination of WO 92/07952 A1 and US 2003/0191286 A1 has been discussed above, hereafter referred to as "the combined references."

The combined references do not teach wherein the determining comprises reading fluorescence using high throughput scanning.

US 20040253632 A1 discloses the "high throughput" screening methods are desired and particular detection formats may be very useful, some examples of which are cell free assays based on optical, fluorescence intensity ([0185]).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adopted a high throughput cell free assay such as disclosed by US 20040253632 A1 in the method of the combined references. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to take advantage of desirable high throughput screening as disclosed by US 20040253632 A1 for the determining step in the cell free assay taught by the combined references.

9. Claims 13, 17, 38 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/07952 A1 (IDS reference filed 7/12/07) in view of US 2003/0191286 A1 as applied to claims 1-9, 11, 20-22, 25-34, 36, 45-47 and 50 above, and further in view of US 20040072262 A1.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The combination of WO 92/07952 A1 and US 2003/0191286 A1 has been discussed above, hereafter referred to as "the combined references."

The combined references do not teach wherein the monomer is HLA-A2/MART-1_{26-35} (claims 13 and 28), nor wherein high throughput scanning is employed in the determining step (claims 17 and 42).

US 20040072262 A1 discloses that the intermediate affinity peptide MART-1_{26-35} showed a very high off rate when complexed to HLA-A2 ([0140]-[0144]). US 20040072262 A1 discloses that having MHC complexes bound to a solid surface is

compatible with high throughput scanning (especially [0070] and claims 4, 31 and 45, abstract, Figure 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the MART-1_{26-35} peptide as the template MHC binding peptide bound to HLA-A2 in the method taught by the combined references.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 92/07952 A1 of the combined references teaches preloading an isolated MHC glycoprotein with a homogeneous peptide preparation, the peptide chosen to be comparatively readily released by the MHC molecule, and US 20040072262 A1 discloses that the intermediate affinity peptide MART-1_{26-35} showed a very high off rate when complexed to HLA-A2.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adopted a high throughput assay such as disclosed by US 20040072262 A1 in the method of the combined references.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to take advantage of desirable high throughput screening as disclosed by US 20040072262 A1 for the determining step in the cell free assay taught by the combined references, particularly in light of the teaching of WO 92/07952 A1 of the combined references that the MHC agonist peptide may be biotinylated and the complex attached to a solid surface via biotin streptavidin linkage.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. In addition, Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 7/12/07 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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January 17, 2008

1/19/08

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